**IN THE SPECIFICATION:**

**Please amend the paragraph beginning on page 26, line 1 as follows:**

The reverse phase HPLC was conducted on a Waters 600 HPLC system on preparative and analytical ~~Vydac~~VYDAC C18 columns. Samples were typically run using a 1% gradient (100% A, 5 min; 100% A to 60% B, 60 min) at 1 ml/min and monitored at 214 nm. Additional fractionation was at times achieved using size-exclusion HPLC. Fractions for assay were collected either at 1 minute intervals or to correspond to peaks detected with a u.v. detector. The buffer system used for all analysis was A=0.1%TFA in $H_2O$ and B=0.09%TFA, 10%$H_2O$, 90%$CH_3CN$.

**Please amend the paragraph beginning on page 28, line 17 as follows:**

A ~~Waters~~WATERS 600 HPLC system equipped with an auto-injector was used for all RP-HPLC. Analytical RP-HPLC was conducted on a ~~Waters~~WATERS Delta pak C18, 300A (0.39 x 30cm) column or a ~~Vydac~~VYDAC C18, 5μ (0.46 x 25cm) column. Samples were run using a 1% gradient (100%A, 5min; 100%A to 60%B, 60min), at 1ml/min and monitored at 214nm. The buffer system used for all analysis was A=0.1%TFA in $H_2O$ and B=0.09%TFA, 10%$H_2O$, 90%$CH_3CN$.

**Please amend the paragraph beginning on page 28, line 24 as follows:**

A ~~Vydac~~VYDAC C18, 5 μ (1.0 x 25cm) column was used for semipreparative RP-HPLC and a ~~Vydac~~VYDAC C18, 10 μ (2.2 x 25cm) column was used for preparative RP-HPLC.
The crude reduced peptides were purified by preparative chromatography, using a 1% gradient (100%A to 80%B, 80min) with a flow rate of 8ml/min and u.v detection at 230nm. Fractions were collected and analysed by electrospray mass spectrometry. Fractions which gave the desired mass were then analysed by analytical RP-HPLC to confirm purity, and those fractions which were pure were combined and lyophilised to give the reduced peptide.

**Please amend the paragraph beginning on page 29, line 10 as follows:**

Mass spectra were measured on a PE ~~Sciex~~SCIEX API-III triple quadrupole Ion Spray mass spectrometer. Data was obtained in the positive ion mode by the accumulation of data in the range 400-2100 amu from several scans using a scan step of 0.1 amu, and a delay time of 0.3 s.

**Please amend the paragraph beginning on page 29, line 21 as follows:**

Other high-resolution data were obtained on a ~~Bruker~~BRUKER Spectrospin BioAPEX external-ion-source Fourier transform electrospray mass spectrometer at a magnetic field of 4.7 T.

**Please amend the paragraph beginning on page 30, line 23 as follows:**

Strand-1 cDNA was 3' end synthesised from the *C. catus* poly-A mRNA templates using a Not1-d$(T)_{18}$ bifunctional primer (5'-AACTGGAAGAATTCGCGGCCGCAGGAAT$_{(18)}$-3')[SEQ ID NO:40] (Pharmacia Biotech) in conjunction with Superscript II reverse transcriptase (Gibco BRL). The resultant cDNA templates were used to manufacture double stranded cDNA using a RNaseH/DNA polymerase procedure as per the Pharmacia Biotech cDNA Timesaver protocol. ~~Marathon~~MARATHON (Clontech) adaptors were then added to the 5' and 3' ends of the ds-cDNA molecules to complete the cDNA construction. A representation of a complete coneshell venom peptide cDNA molecule is shown in figure 1.

**Please amend the paragraph beginning on page 31, line 8 as follows:**

PCR was carried out on samples containing ds-cDNA from *C.catus*, the CSRD-301A primer (5' - ATCATCAAAATGAAACTGACGTC - 3') [SEQ ID NO: 41], the ANCHOR primer (5' - AACTGGAAGAATTCGCGGCCGCAGGAAT - 3') [SEQ ID NO: 42] and an appropriate ~~*Tag*~~ *Taq* polymerase (Biotech International) and buffer (25mM Mg, 100uM deoxy-nucleotides, buffered at pH 8.5) in a thermal cycler (Omnigene) at 95°C/2 mins for 1 cycle, 95°C/30 sec - 55°C/60 sec -72°C/90 sec for 35 cycles, and 72°C/10 mins for 1 cycle. This PCR produced a heterogeneous DNA product of approximately 380 bp to 500bp. Sequence analysis of clones derived from this PCR product have shown it to contain the sequence CVID as well as other related venom peptide sequences.

**Please amend the paragraph beginning on page 31, line 20 as follows:**

The DNA product produced from the CSRD-301A-ANCHOR driven PCR of *C. catus* cDNA was electrophoresed in low melting point agarose and excised. The DNA was extracted from the agarose on Qiagen columns, rephosphorylated with T4 DNA kinase (Progen), blunt ended with Klenow polymerase (Progen), and ligated with T4 DNA ligase (Progen) into the multiple cloning site of dephosphorylated *Sma-1* cut pUC-18 plasmid vector DNA (Pharmacia Biotech). The vector DNA was electrotransformed into Bluescript *E.coli* cells, to produce a library of clones representing the PCR product. Aliquots of the library were plated onto $LB_{amp}$ plates, and individual clones selected and propagated overnight in $TB_{amp}$ broth. Plasmid DNA was purified from the culture using the RPM system (BIO-101), and the PCR DNA inserts within the vector sequenced using the pUC-18 forward and reverse primers (Pharmacia Biotech), di-deoxy terminator sequencing chemistries (Perkin Elmer) on ABI 373 sequencers. The sequence data was analysed using ~~Sequence Navigator~~SEQUENCE NAVIGATOR software (Applied Biosystems).

**Please amend the paragraph beginning on page 33, line 21 as follows:**

Preparative HPLC of $^{125}$I-labelled peptides was performed on a Waters 680 gradient controller equipped with two ~~Waters~~WATERS 510 HPLC pumps and a ~~Waters~~WATERS 481 absorbence detector. Peptides were analysed on ~~Vydac~~VYDAC reverse phase C-18 analytical column (4.6 x 250 mm) eluted at 1 ml/min with a linear gradient of 0-67% of solvent B over 100 min: solvent A, 1% TFA (trifluoroacetic acid); solvent B, 90% ACN + 0.09% TFA. Separation was monitored at 214 nm and 1 ml fractions were collected. Fractions of interest were detected with a LKB Wallac 1272 automatic Gamma counter.

**Please amend the paragraph beginning on page 34, line 6 as follows:**

Rat membrane was prepared according to the procedure of Wagner *et al.* (1988). Rats were sacrificed by cervical dislocation and their brains removed and immediately frozen in liquid nitrogen. Frozen brains were stored at $-78^0$C until required. Three brains (wet weight, 6.25 g) were thawed and homogenised with ~~ultraturrex~~ULTRATURREX homogenizer (IKA, 170 Watt) in 125 ml 50 mM HEPES pH 7.4. Homogenised brain was centrifuged at 16000rpm

(35000g) for 20min at $4^0$C and the supernatant discarded. The pellet was resuspended by further homogenisation in 50mM HEPES, pH 7.4, 10 mM EDTA and incubated at $4^0$C for 30 min. Centrifugation was repeated as above and the supernatant discarded. The pellet was resuspended in 125ml 50mM HEPES, pH 7.4 (1:20 dilution) and stored at $-78^0$C.

**Please amend the paragraph beginning on page 34, line 18 as follows:**

Binding experiments were performed as previously described (Kristipati *et al.*, 1994, Nadasdi *et al.*, 1995). Ligand binding assays were run in triplicate in glass tubes at room temperature. Briefly, assays were performed in 12 x 75 mm borasilicate culture tubes at room temperature and incubated for 1hr. Each tube contained 100 µl each of test compound, iodinated ligand (7 fmol) and rat membrane (16 mg) added in this order. The assay buffer contained 20mM HEPES pH7.2, 75 mM NaCl, 0.1 mM EDTA, 0.1 mM EGTA, 0.1% BSA and protease inhibitors, 2 mM leupeptin and 0.5U aprotinin. The nonspecific binding was determined in the presence of either 17nM GVIA or 100 nM MVIIC. Assays were terminated by vacuum filtration on a Millipore manifold filtration system using glass fibre filters (Whatman GFB) presoaked in 0.6% polyethylenimine. Each tube was washed 3 times with 3ml ice-cold wash buffer (20mM HEPES pH7.2, 125mM NaCl and 0.1% BSA). Filters were counted on a gamma counter. In some instances, potency estimates at the N-type calcium channel were determined by measuring $^{125}$I-GVIA bound to rat brain membrane that was filtered using a Tomtec harvester and counted with a ~~MicroBeta~~MICROBETA Jet scintillation counter. Similar results were obtained with both procedures. In all cases ~~Graphpad Prism~~ the GRAPHAD PRISM program was used to generate binding curves and calculate $EC_{50}$ values. Values for some of the compounds of the present invention are shown in Table 4.

**Please amend the paragraph beginning on page 37, line 23 as follows:**

*Data analysis* - Structures were compared using pairwise and average RMSDs for the Cα, C and N atoms (XPLOR version 3.8), and by calculating angular order parameters for the backbone dihedral angles [Hyberts *et al.*, 1992; Pallaghy *et al.*, 1993]. Structure visualisation was performed using the INSIGHTII program (MSI).